CLAIMS

We claim:

1. A method of inhibiting ztnf4 activity in a mammal comprising administering to said mammal an amount of a compound selected from the group consisting of:

a) a soluble ztnf4 receptor;

b) a polypeptide comprising the extracellular domain of BR43x2;

c) a polypeptide comprising the extracellular domain of TACI;

d) a polypeptide comprising the extracellular domain of BCMA;

e) a polypeptide comprising the sequence of SEQ ID NO:10;

f) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:2;

g) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:4;

h) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:6;

i) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:8;

j) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:10;

k) a polypeptide of SEQ ID NO:4;

l) amino acid residues 1-166 of SEQ ID NO:6; and

m) amino acid residues 1-150 of SEQ ID NO:8.

2. A method according to claim 1, wherein said compound is a fusion protein consisting of a first portion and a second portion joined by a peptide bond, said first portion comprising a polypeptide selected from the group consisting of:

a) a soluble ztnf4 receptor;

b) a polypeptide comprising the sequence of SEQ ID NO:10;

c) a polypeptide comprising amino acid residues 25-58 of SEQ ID NO:2;

d) a polypeptide comprising amino acid residues 34-66 of SEQ ID NO:6;

e) a polypeptide comprising amino acid residues 71-104 of SEQ ID NO:6;

f) a polypeptide comprising amino acid residues 25-104 of SEQ ID NO:6;

g) a polypeptide comprising amino acid residues 8-37 of SEQ ID NO:8;

h) a polypeptide comprising amino acid residues 41-88 of SEQ ID NO:8;

i) a polypeptide comprising amino acid residues 8-88 of SEQ ID NO:8; and

said second portion comprising another polypeptide.

3. A method according to claim 2, wherein said first portion further comprises a polypeptide selected from the group consisting of:

a) amino acid residues 59-120 of SEQ ID NO:2;

b) amino acid residues 105-166 of SEQ ID NO:6; and

c) amino acid residues 89-150 of SEQ ID NO:8.

4. A method according to claim 2, wherein said first portion is selected from the group consisting of:

a) a polypeptide comprising the extracellular domain of BR43x2;

b) a polypeptide comprising the extracellular domain of TACI; and

c) a polypeptide comprising the extracellular domain of BCMA.

5. A method according to claim 2, wherein said first portion is selected from the group consisting of:

a) a polypeptide of SEQ ID NO:4;

b) amino acid residues 1-154 of SEQ ID NO:6; and

c) amino acid residues 1-48 of SEQ ID NO:8.

6. A method according to claim 2, wherein said second portion is an immunoglobulin heavy chain constant region.

7. A method according to claim 1, wherein said antibody or antibody fragment is selected from the group consisting of:

a) polyclonal antibody;

b) murine monoclonal antibody;

c) humanized antibody derived from b); and

d) human monoclonal antibody.

8. A method according the claim 7, wherein said antibody fragment is selected from the group consisting of F(ab'), F(ab), Fab', Fab, Fv, scFv, and minimal recognition unit.

9. A method according to claim 1, wherein said mammal is a primate.

10. A method according to claim 1, wherein said ztnf4 activity is associated with B lymphocytes.

11. A method according to claim 1, wherein said ztnf4 activity is associated with activated B lymphocytes.

12. A method according to claim 1, wherein said ztnf4 activity is associated with resting B lymphocytes.

13. A method according to claim 1, wherein said ztnf4 activity is associated with antibody production.

14. A method according to claim 13, wherein said antibody production is associated with an autoimmune disease.

15. A method according the claim 14, wherein said autoimmune disease is systemic lupus erythomatosis, myasthenia gravis, multiple sclerosis, insulin dependent diabetes mellitus, or rheumatoid arthritis.

16. A method according to claim 1, wherein said ztnf4 activity is associated with asthma, bronchitis or emphysema.

17. A method according to claim 1, wherein said ztnf4 activity is associated with end stage renal failure.

18. A method according to claim 1, wherein said ztnf4 activity is associated with renal disease.

19. A method according to claim 18, wherein said renal disease is glomerulonephritis, vasculitis, nephritis, chronic lymphoid leukemia, or pyelonephritis.

20. A method according to claim 1, wherein said ztnf4 activity is associated with renal neoplasms, multiple myelomas, lymphomas, light chain neuropathy or amyloidosis.

21. A method according to claim 1, wherein said ztnf4 activity is associated with effector T cells.

22. A method according to claim 21, wherein said ztnf4 activity is associated with regulating immune response.

23. A method according the claim 21, wherein said ztnf4 activity is associated with immunosuppression.

24. A method according to claim 23, wherein said immunosuppression is associated with graft rejection, graft verses host disease or inflammation.

25. A method according to claim 24, wherein said immunosuppression is associated with autoimmune disease.

26. A method according to claim 25, wherein said autoimmune disease is insulin-dependent diabetes mellitus or Crohn's disease.

27. A method according to claim 24, wherein said immunosuppression is associated with inflammation.

28. A method according to claim 27, wherein said inflammation is associated with joint pain, swelling, anemia, or septic shock.

29. A method for inhibiting BR43x2, TACI or BCMA receptor-ligand engagement comprising administering an amount of a compound selected from the group consisting of:

a) a soluble ztnf4 receptor;

b) a polypeptide comprising the extracellular domain of BR43x2;

c) a polypeptide comprising the extracellular domain of TACI;

d) a polypeptide comprising the extracellular domain of BCMA;

e) a polypeptide comprising the sequence of SEQ ID NO:10;

f) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:2;

g) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:4;

h) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:6;

i) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:8;

j) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:10;

k) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:18;

l) an antibody or antibody fragment which specifically binds to a polypeptide of SEQ ID NO:20;

m) a polypeptide of SEQ ID NO:4;

n) amino acid residues 1-166 of SEQ ID NO:6; and

o) amino acid residues 1-150 of SEQ ID NO:8.

30. A method according to claim 29, wherein said compound is a fusion protein consisting of a first portion and a second portion joined by a peptide bond, said first portion comprising a polypeptide selected from the group consisting of:

a) a polypeptide comprising the sequence of SEQ ID NO:8;

b) a polypeptide comprising amino acid residues 25-58 of SEQ ID NO:2;

c) a polypeptide comprising amino acid residues 34-66 of SEQ ID NO:6;

d) a polypeptide comprising amino acid residues 71-104 of SEQ ID NO:6;

e) a polypeptide comprising amino acid residues 25-104 of SEQ ID NO:6;

f) a polypeptide comprising amino acid residues 8-37 of SEQ ID NO:8;

g) a polypeptide comprising amino acid residues 41-88 of SEQ ID NO:8;

h) a polypeptide comprising amino acid residues 8-88 of SEQ ID NO:8; and

said second portion comprising another polypeptide.

31. A method according to claim 30, wherein said first portion further comprises a polypeptide selected from the group consisting of:

a) amino acid residues 59-120 of SEQ ID NO:2;
b) amino acid residues 105-166 of SEQ ID NO:6; and
c) amino acid residues 89-150 of SEQ ID NO:8.

32. A method according to claim 30, wherein said first portion is selected from the group consisting of:

a) a polypeptide comprising the extracellular domain of BR43x2;

b) a polypeptide comprising the extracellular domain of TACI; and

c) a polypeptide comprising the extracellular domain of BCMA.

33. A method according to claim 30, wherein said first portion is selected from the group consisting of:

a) a polypeptide of SEQ ID NO:4;
b) amino acid residues 1-154 of SEQ ID NO:6; and
c) amino acid residues 1-48 of SEQ ID NO:8.

34. A method according to claim 30, wherein said second portion is an immunoglobulin heavy chain constant region.

35. A method according to claim 29, wherein said antibody or antibody fragment is selected from the group consisting of:

a) polyclonal antibody;
b) murine monoclonal antibody;
c) humanized antibody derived from b); and
d) human monoclonal antibody.

36. A method according the claim 35, wherein said antibody fragment is selected from the group consisting of F(ab'), F(ab), Fab', Fab, Fv, scFv, and minimal recognition unit.

37. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with B lymphocytes.

38. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with activated B lymphocytes.

39. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with resting B lymphocytes.

40. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with antibody production.

41. A method according to claim 40, wherein said antibody production is associated with an autoimmune disease.

42. A method according the claim 41, wherein said autoimmune disease is systemic lupus erythematosis, myasthenia gravis, multiple sclerosis, insulin dependent diabetes mellitus, or rheumatoid arthritis.

43. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with asthma, bronchitis or emphysema.

44. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with end stage renal failure.

45. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with renal disease.

46. A method according to claim 45, wherein said renal disease is glomerulonephritis, vasculitis, nephritis, chronic lymphoid leukemia, or pyelonephritis.

47. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with renal neoplasms, multiple myelomas, lymphomas, light chain neuropathy or amyloidosis.

48. A method according to claim 29, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with effector T cells.

49. A method according to claim 48, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with regulation of immune response.

50. A method according the claim 49, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with immunosuppression.

51. A method according to claim 50, wherein said immunosuppression is associated with graft rejection, graft verses host disease or inflammation.

52. A method according to claim 50, wherein said immunosuppression is associated with autoimmune disease.

53. A method according to claim 52, wherein said autoimmune disease is insulin-dependent diabetes mellitus or Crohn's Disease.

54. A method according to claim 50, wherein said BR43x2, TACI or BCMA receptor-ligand engagement is associated with inflammation.

55. A method according to claim 54, wherein said inflammation is associated with joint pain, swelling, anemia, or septic shock.

56. An isolated polynucleotide molecule encoding a polypeptide of SEQ ID NO:2.

57. An isolated polynucleotide molecule of SEQ ID NO:1.

58. An expression vector comprising the following operably linked elements:

a transcription promoter;

a polynucleotide molecule according to claim 56; and

a transcription terminator.

59. A cultured cell into which has been introduced an expression vector according to claim 58, wherein said cultured cell expresses said polypeptide encoded by said polynucleotide segment.

60. A method of producing a polypeptide comprising:

culturing a cell into which has been introduced an expression vector according to claim 58;

whereby said cell expresses said polypeptide encoded by said polynucleotide molecule; and

recovering said expressed polypeptide.

61. An isolated polypeptide having the sequence of SEQ ID NO:2.

62. A polypeptide of claim 61, in combination with a pharmaceutically acceptable vehicle.

63. A method for regulating B lymphocytes in a recipient in need of such B lymphocyte regulation, comprising

administering to said recipient a pharmaceutically effective amount of a soluble ztnf4 receptor in a pharmaceutically acceptable vehicle.

64. A method according to claim 63, wherein said B lymphocyte regulation is selected from the group consisting of:

a) inhibition of B lymphocyte proliferation;
b) inhibition of B lymphocyte activation;
c) inhibition of B lymphocyte homeostasis; and
d) inhibition of B lymphocyte effector function.

65. A method according to claim 63, wherein said B lymphocyte regulation is modulation of autoantibody production.

66. A method according to claim 63, wherein said B lymphocyte regulation is the reduction of B lymphocytes in the periphery of said recipient.

67. A method of claim 63, wherein said B lymphocytes are pre-pro or immature B lymphocytes.

68. A method according to claim 63, wherein said B lymphocyte regulation is associated with an autoimmune disease.

69. A method according the claim 68, wherein said autoimmune disease is systemic lupus erythematosis, myasthenia gravis, multiple sclerosis, insulin-dependent diabetes mellitus, or rheumatoid arthritis.

70. A method according to claim 63, wherein said B lymphocyte regulation is associated with asthma, bronchitis or emphysema.

71. A method according to claim 63, wherein said B lymphocyte regulation is associated with end stage renal failure.

72. A method according to claim 63, wherein said B lymphocyte regulation is associated with renal disease.

73. A method according to claim 71, wherein said renal disease is glomerulonephritis, vasculitis, nephritis, chronic lymphoid leukemia, or pyelonephritis.

74. A method according to claim 63, wherein said B lymphocyte regulation is associated with renal neoplasms, multiple myelomas, lymphomas, light chain neuropathy or amyloidosis.

75. A method according to claim 63, wherein B lymphocyte regulation is associated with effector T cells.

76. A method according to claim 75, wherein said B lymphocyte regulation is associated with regulation of immune response.

77. A method according the claim 76, wherein said B lymphocyte regulation is associated with immunosuppression.

78. A method according to claim 77, wherein said immunosuppression is associated with graft rejection, graft verses host disease or inflammation.

79. A method according to claim 76, wherein said B lymphocyte regulation is associated with autoimmune disease.

80. A method according to claim 79, wherein said autoimmune disease is insulin-dependent diabetes mellitus or Crohn's Disease.

81. A method according to claim 63, wherein said B lymphocyte regulation is associated with inflammation.

82. A method for reducing proteinuria in a recipient in need of such reduction, comprising administering to said recipient a pharmaceutically effective amount of a soluble ztnf4 receptor in a pharmaceutically acceptable vehicle.

83. A method of claim 82, wherein said proteinuria is stimulated by ztnf4.

84. A method of claim 82, wherein said proteinuria is associated with an autoimmune disease.

85. A method according the claim 84, wherein said autoimmune disease is systemic lupus erythomatosis, myasthenia gravis, or rheumatoid arthritis.

86. A method according to claim 82, wherein said proteinuria is associated with end stage renal failure.

87. A method according to claim 82, wherein said proteinuria is associated with renal disease.

88. A method according to claim 87, wherein said renal disease is glomerulonephritis, vasculitis, nephritis, chronic lymphoid leukemia, or pyelonephritis.

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